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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/528,978	03/21/00	OBACH	R PC10244A

023913
PFIZER INC
150 EAST 42ND STREET
5TH FLOOR - STOP 49
NEW YORK NY 10017-5612

HM12/0814

EXAMINER	
JIANG,S	
ART UNIT	PAPER NUMBER
1617	5

DATE MAILED: 08/14/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/528,978	OBACH, R. SCOTT	
	Examiner	Art Unit	
	Shaojia A. Jiang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 July 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *2-3, 5,7-10,and 12-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4, 6 and 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This application claims priority to provisional application Serial No. 60/128,136.

Election/Restrictions

Applicant's amendment and election with traverse of the invention of Group I, Claims 1-13 and elected species of (2S,3S)-2-phenyl-3-(2-methoxy-5-trifluoromethoxyphenyl)methylamino-piperidine in claim 6 and quindine in claim 11 in Paper No. 4, submitted July 26, 2001 is acknowledged.

The traversal is on the ground(s) that inventions Groups I and II are related to each other and have same functions. This is found persuasive as to Groups I and II have same functions. However, inventions Group II and I are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, for example, Zonisamide in combined with nicardipine may be used in the instant claimed method.

Therefore, inventions of Groups II and I are independent and distinct each from other since they are related as product and process of use as discussed above and an undue burden on the Office is seen for the search all inventions herein. Note that the search is not limited to patent files. Note that the search field for a composition

employing a combination of agents is different from the search field for a specified method of use employing the same combination of agents.

The requirement is still deemed proper and is therefore made FINAL.

Claims 14-22 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 2-3, 5, 7-10, and 12-13 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim.

The requirement is therefore made FINAL.

The claims have been examined insofar as they read on the elected specie.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 4, 6, and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Benet et al. (A, PTO-892) and Hess (U, PTO-892).

Benet et al. teaches the administration a drug that is the particular cytochromes P450, CYP2D6 substrate which is a member of CYP family, in mediating oxidative

biotransformation for the major clearance mechanism in humans. See col.1-2. Benet et al. also teaches that CYP2D6 inhibitors such as quinidine, calcium channel blockers, and phenothiazines are useful as bioenhancers to increase the bioavailability of a pharmaceutical compound through the inhibition of cytochrome P450. See col.2 lines 46 – col.3 lines 25, and col.7. Benet et al. further teaches that a drug having activity of CYP3A (CYP3A substrate), another particular member of CYP family in combination with a CYP3A inhibitor which is not the same compound in the instant method for the improvement of drug bioavailability and major clearance. See col.9-11 Table 1.

Hess discloses that the instant elected species, (2S,3S)-2-phenyl-3-(2-methoxy-5-trifluoromethoxyphenyl)methylamino-piperidine, is a NK-1 receptor antagonist containing a secondary alkylamine. See abstract, page 22, lines 24-25, and page 152 lines 33-34 (claim 10).

The prior art does not expressly disclose the employment of (2S,3S)-2-phenyl-3-(2-methoxy-5-trifluoromethoxyphenyl)methylamino-piperidine as a CYP2D6 substrate in mediating oxidative biotransformation in combination with quinidine as a CYP2D6 inhibitor to be administered in a method for the major clearance mechanism in humans.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ (2S,3S)-2-phenyl-3-(2-methoxy-5-trifluoromethoxyphenyl)methylamino-piperidine as CYP2D6 in mediating oxidative biotransformation in combination with quinidine as a CYP2D6 inhibitor to be administered in a method for the major clearance mechanism in humans.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ (2S,3S)-2-phenyl-3-(2-methoxy-5-trifluoromethoxyphenyl)methylamino-piperidine as a CYP2D6 substrate in mediating oxidative biotransformation in combination with quinidine as a CYP2D6 inhibitor to be administered in a method for the major clearance mechanism in humans since NK-1 receptor antagonists are well known CYP2D6 substrates. It is well known that CYP2D6 substrates mediate oxidative biotransformation for the major clearance mechanism in humans. Moreover, quinidine is well known to be a CYP2D6 inhibitor, useful in a method for enhancing drug pharmacokinetic profile and the major clearance mechanism. Further, it is known that the employment of a drug having CYP3A activity within the same CYP family (a CYP3A substrate) in combination with a CYP3A inhibitor which is not the same compound is useful in the same method for improvement of the improvement of drug bioavailability and major clearance according to Benet et al. Therefore, one of ordinary skill in the art would have reasonably expected that combining (2S,3S)-2-phenyl-3-(2-methoxy-5-trifluoromethoxyphenyl)methylamino-piperidine, a CYP2D6 substrate, in combination with quinidine, a CYP2D6 inhibitor, known useful for the same purpose in a composition to be administered would be useful for the instant claimed method as same as the combination of a CYP3A substrate and a CYP3A inhibitor does. Since all active composition components herein are known, it is considered prima facie obvious to combine them into a single composition useful for the very same purpose. See *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980).

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

In view of the rejections to the pending claims set forth above, no claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (703) 305-1008. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Minna Moezie, J.D., can be reached on (703) 308-4612. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-1235.

Shaojia A. Jiang, Ph.D.
Patent Examiner, AU 1617
August 6, 2001

MINNA MOEZIE, J.D.
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600